in this application. For the convenience of the Examiner, an appendix of pending claims is attached hereto.

The Advisory Action also states that the rejections under 35 U.S.C. §102(e) and §103(a) are overcome by the After Final Amendment filed December 23, 1999. However, the Advisory Action states that claims 27-31 lack proper antecedent basis and that claims 31 and 39 are indefinite with regard to the location of a terminator sequence within an expression cassette. The Advisory Action also states that the written description and scope rejections are maintained.

Support for the Amendments

Claims 22, 27, 29, 30, 31 and 39 are amended to correct a minor typographical error or to further clarify the invention. For example, claims 27, 29, 30 and 31 are amended to change the dependencies of the claims. Support for amendments to claims 30 and 39 can be found on, *e.g.*, Figure 8. Support for new claim 41 can be found in, *e.g.*, originally filed claim 10. No new matter has been introduced by these amendments.

The Rejections under 35 U.S.C. §112, First Paragraph

A. Written Description Rejection

The Advisory Action states that the written description rejection is maintained, because "Applicants have not isolated other isolated anti-bacterial genes or taught how to isolate other anti-bacterial genes from a Diptera insect, other than sarcotoxin 1a gene." The Advisory Action does not state which new claims are being rejected under the written description rejection. However, in light of the above quoted statement, Applicants assume that the Examiner is applying the rejection to claims 21, 22, 24-33 and 35-41, which do not recite Sarcotoxin 1a. Applicants respectfully traverse this rejection.

Applicants respectfully submit that an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). *See, also*, MPEP §2163.02. An Applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as

words, structures, figures, diagrams, formulas, *etc.* that set forth the claimed invention." *See, e.g., University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997).

Here, the description in the instant specification clearly allows persons of ordinary skill in the art to recognize that Applicants invented what is claimed. For example, claim 21 is directed to "a method of conferring resistance to pathogenic fungi on a plant using a DNA sequence encoding an anti-bacterial peptide from a Diptera insect, the method comprising the steps of: transforming a plant cell by introducing the DNA sequence encoding the anti-bacterial peptide from the Diptera insect; and regenerating the transformed plant cell into a transgenic plant expressing the anti-bacterial peptide." The specification provides an adequate written description for this claimed invention. For example, page 15, second paragraph, of the specification provides support for transforming a plant with a gene encoding an anti-bacterial peptide derived from a Diptera insect to confer resistance to pathogenic fungi in a plant. Page 10, line 12 of the specification provides Sarcotoxin 1a as one embodiment of the anti-bacterial peptide derived from a Diptera insect. In light of these disclosures, persons of ordinary skill in the art would have recognized that Applicants invented what is claimed, *e.g.*, in claim 21.

In rejecting the present claims, the Examiner appears to rely on the decision in *University of California v. Eli Lilly*, 43 USPQ2d 1398 (Fed. Cir. 1997) and to allege that the claimed genus of anti-bacterial genes is not adequately described. As noted in the previous Amendments, the claimed invention is not directed at particular sequences or nucleic acids, but their use in new methods and plants that contain a particular expression vector comprising these nucleic acids. For example, new claims 21-31 are directed to *methods* of conferring resistance to pathogenic fungi on a plant using a DNA sequence encoding an anti-bacterial peptide from a Diptera insect. The novelty of the instant claims is not based on the discovery of a new class of nucleic acids (as was the case in *University of California*). Rather, it is based at least in part on the surprising discovery that anti-bacterial genes can be used in a method to confer anti-fungal properties on transgenic plants comprising them. As such, the facts of the instant case are not analogous to the facts in *University of California*. Accordingly, the holding in *University of California* does not apply to the instant case.

Similarly, the inventive aspect of claims 32-40 is not based on the discovery of new class of nucleic acids. New claims 32-40 are directed to a plant comprising an anti-bacterial gene from a Diptera insect, wherein the plant confers resistance to pathogenic fungi. The inventive aspect lies in part on the positioning of an inducible promoter and a constitutive promoter in an expression vector and its effect on the anti-bacterial gene expression. Specifically, when an inducible promoter which is operably linked to an anti-bacterial gene is positioned adjacent to a constitutive promoter, the constitutive expression of the anti-bacterial gene is observed under the influence of a constitutive promoter. Moreover, the expression is increased by adding an agent that induces the inducible promoter. *See*, page 11, last line to page 12, line 16 of the specification. Therefore, the inventive aspect of claims 32-40 is not based on the discovery of new class of nucleic acids as in *University of California*. Accordingly, the written description requirement of nucleic acid sequences set forth in *University of California* is inapplicable to these claims.

Even if the anti-bacterial gene sequences were the inventive aspect of the present claims, Applicants respectfully remind the Examiner that the specification need not disclose all species encompassed by the claimed invention to satisfy the written description requirement of 35 U.S.C. §112, first paragraph. As clearly stated by the Court of Appeals for the Federal Circuit, "[a] specification may, within the meaning of §112, ¶ 1, containing a written description of a broadly without describing all species that claim encompasses." *Utter v. Hiraga*, 6 USPQ2d 1709 (Fed. Cir. 1988). *See, also, University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). If "all" species encompassed by the claims must be described to satisfy the written description requirement, no generic claim would ever be allowable.

For these reasons, the rejection is improper for the claims, as previously presented or currently pending. Withdrawal of the rejection is respectfully requested.

B. Enablement

The Advisory Action states that the enablement rejection is maintained. The Advisory Action further states that "Applicants does not teach which other anti-bacterial genes would provide anti-fungal effect in transgenic plants. In view of the single example and unexpected results of Applicants, undue trial and error experimentation would be required to

identify other genes which could be used in the claimed methods and transgenic plants." Applicants respectfully traverse this rejection.

As an initial matter, it is noted that claims 23 and 34 recite the limitation "Sarcotoxin 1a." Applicants believe that the written description and enablement rejections were not maintained for these claims in the Advisory Action. Accordingly, claims 23 and 34 are allowable, and a notice to that effect is respectfully requested.

The proper test of enablement is "whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation." *United States v. Teletronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). MPEP §2164.01. In the instant case, the Examiner appears to require that other examples of anti-bacterial peptide conferring anti-fungal effect in transgenic plants are required. It is respectfully submitted that the Examiner's requirement that other examples be provided in the specification is not a basis, let alone a reasonable basis, to request the enablement provided in the claimed invention. Although the Examiner alleges that other examples are lacking, no basis in the law or evidence has been provided as to why the examples are critical to make and use the claimed invention in view of the specification. Therefore, a *prima facie* case of non-enablement has not been established, and the rejection should be withdrawn for this reason alone.

Moreover, as noted in the previous Amendments, enablement is not precluded by the necessity of some experimentation, such as routine screening. As the Court of Appeals for the Federal Circuit stated: "the key is 'undue', not 'experimentation'" in determining whether pending claims are enabled. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). This decision makes clear that a considerable amount of experimentation is permissible if it is merely routine, or if the specification provides a reasonable amount of guidance respect to the direction in which the experimentation should proceed.

Applicants respectfully submit that the Examiner's requirement to limit the claims to Sarcotoxin 1a is unduly restrictive, because a number of other anti-bacterial peptides from a Diptera insect were well known as of the instant filing date. For example, Wicker *et al.* describes that several families of bacterial peptides have been isolated from immune insects, including, *e.g.*, ceprocins, attacins, dipericins, insect defensins, apidaecins and various

homologues referred to as Sarcotoxins and sapecins. (*see, e.g.*, page 22493, first column of *J. Bio. Chem.*, 25:22493-8 (1990), attached with the After Final Amendment filed December 23, 1999). In light of this, those skilled in the art would have been able to introduce into a plant various anti-bacterial genes from a Diptera insect, other than Sarcotoxin Ia, without undue experimentation.

Applicants also submit that the experimentation necessary to identify a working embodiment of the invention (*i.e.*, an anti-bacterial peptide from a Diptera insect that confers fungal resistance) other than Sarcotoxin 1a is not undue. It is a simple matter to screen for working embodiments of Diptera anti-bacterial genes using the routine screening methods as taught in the present specification. For example, Example 7 of the specification describes *in vitro* methods for measuring an anti-fungal activity of Diptera anti-bacterial peptides. Specifically, each petri dish of a suitable medium is inoculated with a pathogenic fungi (*e.g.*, *Fusarium oxysporum F-3*, *Rhizoctonia solani*, or *Rizoctonia solani AG-4*) and the size of each hypha growing is measured. A Diptera anti-bacterial peptide that exhibits anti-fungal activity can be screened by identifying a peptide that reduces the fungal growth, *e.g.*, in a concentration dependent manner. Moreover, Examples 8-10 describe methods for measuring anti-fungal activity of an anti-bacterial peptide from a Diptera insect using transgenic plants. For example, as described in Examples 8 and 9, young transgenic plants growing in petri dishes are inoculated by pathogenic fungi. After several days of incubation, green surviving or healthy plants can be identified as resistant plants. Furthermore, as described in Example 10, the size of brown lesions in transgenic plant leaves that are inoculated with pathogenic fungi can be measured to determine whether an anti-bacterial peptide possesses anti-fungal activity. The identification by Applicants of a Diptera anti-bacterial gene that possesses anti-fungal activity (*e.g.*, Sarcotoxin 1a) using routine experimentation as described above provides strong evidence that other anti-bacterial peptide that confers anti-fungal activity can also be identified with the same routine methods.

Identifying Diptera anti-bacterial genes that possess anti-fungal activity does not require anything other than routine cloning and screening of expression products. Such simple screening procedures have never been considered "undue" experimentation by the courts or the Patent Office. Indeed, a rejection of a claim for undue breadth/lack of enablement

has always been considered inappropriate when "one of skill could readily determine any one of the claimed embodiments." *See*, MPEP § 2164.08. This standard is further explained in the "Training Materials for Examining Patent Applications with Respect to 35 USC Section 112, First Paragraph-Enablement Chemical/Biotechnological Applications" at sections 3.A.2.b.i.(c). The Office explains that, for instance, "even though a listing of all of the possible DNAs which encode a given protein is a practical impossibility due to the enormous number of such nucleic acids, any *particular* sequence can be written by one of skill given the disclosure and the sequence can be ordered from a company which synthesizes DNA." Similarly, in the present case, any desired nucleic acid encoding a Diptera anti-bacterial sequence, as recited in the claims, can be ordered from a commercial source or created using standard cloning techniques. These nucleic acids can subsequently be tested for activity using the simple methods taught in the specification. Nothing articulated by the rejection contradicts this clear indication of the ability of one of skill to readily determine the operability of any potential claimed embodiment. Thus the claims, as previously presented or currently pending, are clearly enabled. Accordingly, withdrawal of the rejection is respectfully requested.

The Rejection under 35 U.S.C. §112, Second Paragraph

The Advisory Action states that claims 27-31 lack proper antecedent basis and that claims 31 and 39 are indefinite regarding the location of a terminator in an expression cassette. Applicants have amended claims 22, 27, 29, 30, 31 and 39 as noted above. Applicants believe that these amendments provide proper antecedent basis and/or the location of a terminator sequence in an expression vector. Accordingly, withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (415) 576-0200.

Respectfully submitted,

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APPENDIX

21. A method of conferring resistance to pathogenic fungi on a plant using a DNA sequence encoding an anti-bacterial peptide from a Diptera insect, the method comprising the steps of: transforming a plant cell by introducing the DNA sequence encoding the anti-bacterial peptide from the Diptera insect; and regenerating the transformed plant cell into a transgenic plant expressing the anti-bacterial peptide.

22. The method according to claim 21, wherein the pathogenic fungi are *Rhizoctonia solani*, *Pythium aphanidermatum*, and *Phytophthora infestans*.

23. The method according to claim 21, wherein the anti-bacterial peptide from the Diptera insect is Sarcotoxin Ia.

24. The method according to claim 21, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is introduced into the plant cell in a form of an expression vector comprising an expression cassette comprising the DNA sequence encoding the anti-bacterial peptide from the Diptera insect operably linked to a first plant promoter and a drug resistance gene operably linked to a second plant promoter which is constitutively expressed, wherein the first promoter and the second promoter are positioned adjacent to each other.

25. The method according to claim 21, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a plant gene via a hinge region of a tobacco chitinase gene.

26. The method according to claim 21, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a signal sequence from a plant gene.

27. The method according to claim 24, wherein the first plant promoter is an inducible promoter.

28. The method according to claim 27, wherein the inducible promoter is a promoter induced by stress.

29. The method according to claim 28, wherein the promoter induced by stress is a promoter of the tobacco PR-1a gene.

30. The method according to claim 24, wherein the expression cassette has a terminator of the tobacco PR-1a gene downstream of the DNA sequence encoding the anti-bacterial peptide from the Diptera insect.

31. The method according to claim 24, wherein the constitutively expressed promoter is the Cauliflower mosaic virus 35S promoter.

32. A plant which confers resistance to pathogenic fungi, the plant comprising an expression vector comprising an expression cassette comprising a DNA sequence encoding an anti-bacterial peptide from a Diptera insect operably linked to an inducible promoter and a drug resistance gene operably linked to a constitutively expressed promoter, wherein the inducible promoter and the constitutively expressed promoter are positioned adjacent to each other.

33. The plant according to claim 32, wherein the pathogenic fungi are *Rhizoctonia solani*, *Pythium aphanidermatum* and *Phytophthora infestans*.

34. The plant according to claim 32, wherein the anti-bacterial peptide from the Diptera insect is Sarcotoxin Ia.

35. The plant according to claim 32, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a plant gene via a hinge region of a tobacco chitinase gene.

36. The plant according to claim 32, wherein the DNA sequence encoding the anti-bacterial peptide from the Diptera insect is operably linked to a signal sequence from a plant gene.

37. The plant according to claim 32, wherein the inducible promoter is a promoter induced by stress.

38. The plant according to claim 37, wherein the promoter induced by stress is a promoter of the tobacco PR-1a gene.

39. The plant according to claim 32, wherein the expression cassette has a terminator of the tobacco PR-1a gene downstream of the DNA sequence encoding the anti-bacterial peptide from the Diptera insect.

40. The plant according to claim 32, wherein the constitutively expressed promoter is the Cauliflower mosaic virus 35S promoter.

41. The plant according to claim 32, wherein the expression vector further has a T-DNA region and a drug resistant gene.